The Department of Defense Pharmacoeconomic Center
PEC UPDATE
January 2003, Vol. 03, Issue 3, www.pec.ha.osd.mil

In This Issue . . .

Last Issue

New Drug Watch

This month: new agents for ADHD and osteoporosis, a combination vaccine (diphtheria, tetanus, pertussis, hepatitis B, and polio), a handful of new formulations and indications, generic omeprazole, FDA alerts, updated neonatal group B streptococcus prophylaxis recommendations and results of some notable trials, including ALLHAT (the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial).

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PDTS Corner

Update on the Pharmacy Data Transaction Service

- **PDTS – Looking Ahead While Glancing Back** - **PDTS processed over 100 MILLION transactions and detected more than 39,000 potential level 1 drug-drug interactions in Calendar Year 2002. Roger Williams, PDTS CSSC Clinical Support Supervisor, tells us what's coming for 2003.**
- **PDTS Data Integrity: a 2002 Review** - **Teresa Howell, PDTS CSSC Clinical Support Coordinator (her unofficial title is "Data Integrity Guru") looks back on 2002 with words of praise—and some helpful hints for improvement. After all, data can never have too much integrity...**
- **Business Objects Class Schedule** - **The capability to run reports on data in the PDTS Data Warehouse is now available to managers at various levels of DoD Pharmacy by using Business Objects software via an Internet Web Server. About twice a month, the PDTS CSSC offers training sessions in Business Objects at Ft Sam Houston, Texas.**
- **Top 10 Level 1 Drug-Drug Interactions** - **Rankings by number of level 1 DDIs reported in each point of service.**
- **Top 50 Drugs for November 2002 by Point of Service** - **Rankings by prescription counts. What's #1 across the system? It isn't a statin, or even a brand name drug—it's generic ibuprofen 800 mg.**

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Coming Up

Report on the 2003 DoD Pharmacoeconomics and Pharmacy Benefit Conference

Excellent Quote of the Month

" If the PEC throws a temper tantrum no one watches; the best we can hope to do is get someone else to throw a tantrum that people will actually pay attention to."

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PEC Update Information

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published in the *PEC Update*? Just send CAPT Torkildson or Shana Trice an e-mail, or call the PEC at DSN 421-1271, Commercial (210) 295-1271.

Publication Schedule

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EDITORIAL

Where Does All the Money Go?

CAPT Joe Torkildson, MC, USN
Director, Clinical Operations Division
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Editors' Letters

Please send your letters to the editors to Dr. Torkildson at **Joseph.Torkildson@amedd.army.mil**

First off, I would like to thank everyone for the kind words sent back to me regarding my last editorial. I realize it wasn't terribly pharmacy or business oriented, but I enjoyed writing it, and I'm glad it was well received by so many of you. But, now that 2003 is upon us, it's time to get back to business. What better way to start off the New Year than to revisit the last of Dr. Roach's **Barb's Barbs** columns, and explore one reader's response to that effort?

A few weeks ago I received a letter from one of our readers that raised a number of interesting questions in response to the December **Barb's Barbs**. However, as this is an editorial I'm going to take the liberty of raising the questions and then exploring what I perceive as the attitudes that underlie them, because I find these even more fascinating than the questions themselves. To refresh everyone's memories, last month's **Barb's Barbs** column (and the one previous) had discussed the ethics of accepting food and other gifts from pharmaceutical representatives, and the accuracy of some of the rationales that many of us employ when justifying such behavior.

Our reader, a senior civilian physician, seemed to take exception both with the general tone of the column, and with several of the points that he felt were made. After asserting that Dr. Roach "missed the most important part of the argument", he goes on to say:

> "Why are the drug companies here detailing drugs with food? Yes, they have a product to sell. However, they are the only ones interested in influencing the physicians through non-coercive means. The PEC can, for all the right reasons, coerce and order physicians to use whatever drugs they feel are the most cost-effective. However, there is no 'money behind the mouth' to get Pharm D's and local speakers into the MTF's to use the very tools of non-coercive influence that you so strongly decry in your article."

Let's start with the part about "influencing the physicians through non-coercive means". Ever since we threw our first temper tantrum in the grocery store we've been trying through one manner or another to change someone else's behavior. And nine times out of ten, the person whose behavior is being tweaked perceives our efforts as being coercive. From our legal system to performance appraisals to the complex mating rituals that take place between partners in a relationship, we see examples of coerced behavior. It makes sense. It is

effective, efficient and inexpensive. Its major drawback is that it makes the people whose behavior is being influenced variably angry and resentful depending on the intrusiveness of the coercion on their regular patterns of behavior. (I'll throw in a brief parenthetical correction here. The PEC does not coerce or order anyone to do anything. Policies that constrain behavior are established elsewhere, formulary decisions that limit choice are made by the DoD P&T Committee, and closed class pharmaceutical contracts are awarded by the Defense Supply Center in Philadelphia after the DoD P&T Committee has decided that it is clinically appropriate to do so. If the PEC throws a temper tantrum no one watches; the best we can hope to do is get someone else to throw a tantrum that people will actually pay attention to.)

On the other side of the coin we have advertising. Advertising is defined in many different ways; the definition I find most illuminating is:

> "Advertising is a paid form of communicating a message by the use of various media. It is *persuasive, informative, and designed to influence purchasing behavior or thought patterns*." (The emphasis is mine.)

Advertising is simply a different means of accomplishing the same end. The big advantage of advertising is that the worst negative emotion usually created is irritation, and this is usually related to the quality of the delivery rather than the quality of the message. People typically don't feel coerced by advertising; they perceive they are always free to simply walk away and not change their behavior if they are not persuaded by the message. The downside of advertising is that it is very expensive relative to coercive means, because it needs to be personal in order to be effective. Each individual must feel the message is speaking to him or her directly. Pharmaceutical companies collectively spend billions of dollars a year in this type of activity—dollars that must be deducted from the bottom line. So advertising has to be very effective in order to be cost effective. This is the challenge facing pharmaceutical representatives. They need to get out into the field and persuade lots of prescribers to choose their product. They have no opportunity to use coercive means, because they have no power advantage over their customers, so they must use advertising. They have to do it effectively; every dollar spent on such advertising has to return substantially more than that in increased revenue. And most of them realize they must do it honestly; the FDA has little patience for reps or companies that attempt to influence behavior using false claims. It is against that backdrop that pharmaceutical reps walk into your facilities to bring lunch.

So what does this mean to you? It should mean that you recognize that the pharmaceutical rep's first job is not to help you treat your patients more safely, effectively, or cheaply; it's to persuade you to use his or her product. That's not good or bad, that's just reality; that's why he or she draws a paycheck from the company. If the company's product is clearly superior to the competition, if in effect it "sells itself", the rep's job is easy. However, if the product is just another in a sea of competitors in terms of efficacy, safety, and tolerability, the rep's job is much more difficult. In order to be successful, they must convince you that their commodity product is differentiated from the rest. And the challenge for you is that they don't come into your facility with materials that state for one product "this is a Lexus" (and it is), and for another product state "this is corn flakes" (which it is). Both will come billed as a Lexus; it is up to you to distinguish the difference. That was the message in Barb's column. There is nothing wrong with pharmaceutical companies sponsoring grand rounds or other educational efforts and bringing food as part of that sponsorship, as long as it's done ethically. That was Barb's message as well. But since the choice of which product to use is being left to you, the onus is on you to choose wisely. And there are plenty of examples within our system of pharmaceutical companies being very effective in convincing prescribers that their product is a Lexus instead of corn flakes.*

This is getting incredibly long, but I did want to make one other point. Our writer's comment, "there is no 'money behind the mouth' to get Pharm D's and local speakers into the MTF's to use the very tools of non-

coercive influence that you so strongly decry in your article" was later explained as decrying the fact that the PEC did not take some of these dollars that are being saved and use them to bring speakers into facilities to counter-detail the pharmaceutical companies. Counter-detailing is a challenging topic; it is advertising just like the drug companies use, with the same advantages and disadvantages (including a relatively healthy price tag). But that's not really the point; the point is really the basis for the title of this editorial. If we convince the DoD P&T Committee that it is clinically appropriate to enter into a contract in a particular drug class, and that contract results in a $10 million cost avoidance for DoD in the first year, **we don't get that money**. Our budget doesn't go up one penny the next year as a result of that maneuver, and there is no slush fund that facilities are required to contribute to if they "save money" based on a procurement strategy. That money is in your facility, and it stays in your facility. So if you think about it critically, the collective behavior of prescribers in each of your facilities has everything to do with how your pharmacy expenditures play out. Every dime that MTFs didn't spend last year because their prescribers wrote prescriptions for rabeprazole instead of omeprazole stayed right at home.

So I would suggest that it's up to you to decide whether you have opportunities at your facility to stretch your pharmacy budget without compromising the care of patients by getting your prescribers to distinguish between cars and corn flakes, and in the latter case to be aware that there really isn't any value in paying three times as much for Brand Y as for Brand X. Then it's up to you to decide how you want to change your prescriber's behavior to bring about that change. Do you want to participate on the counter-detailing team that goes to prescribers identified as having questionable prescribing practices and tries to persuade them to change? Or perhaps you can broker an arrangement between your local P&T Committee and your Executive Committee of the Medical Staff (or equivalent group) to make some aggressive local formulary decisions to move prescribing practice in the desired direction. And if the last choice seems too coercive to you, look on the bright side: at least when you throw a temper tantrum, someone will listen.

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[**Note**: If you're baffled by the Lexus and the cornflakes (I was): the contrast is between products that are differentiated from one another on quality (brand identity) and products that are perceived as interchangeable (no brand identity). I asked Dr. T how he would classify a Lexus filled with cornflakes, but he only rolled his eyes and maintained a dignified silence. ST]

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DoD P&T Highlights

News from the 20 - 21 November 2002 meetings of the DoD Pharmacy &Therapeutics (P&T) Executive Council and the DoD P&T Committee

Shana Trice, Clinical Pharmacy Specialist
DoD Pharmacoeconomic Center

Time for another "Cliff Notes" version of the last DoD P&T meeting minutes—for more details, see the complete minutes of the DoD Pharmacy & Therapeutics (P&T) Committee and the DoD P&T Executive Council meetings on the PEC website at **www.pec.ha.osd.mil/PT_Committee.htm.** The next meetings are scheduled for 6 - 7 March, 2003, at Fort Sam Houston, Texas. Items for the agenda should be submitted to the co-chairs no later than 14 February 2003.

Quick Links

DoD P&T Executive Council Meeting (20 Nov 2002)

BCF changes

- **Added to the BCF:**
  - niacin extended release (Niaspan; Kos) - replaces niacin immediate release
  - norethindrone/ethinyl estradiol/ferrous fumarate 1/0.02/75 mg (Loestrin FE or generic equivalent) - a low estrogen oral contraceptive
  - timolol maleate 0.25% and 0.5% gel-forming solution (specific product Timoptic XE) - although this product is generically available, a mandatory source contract is in effect for the Merck brand (Timoptic XE)
  - tolterodine extended release (Detrol LA; Pharmacia)
  - venlafaxine extended release (Effexor XR; Wyeth)
- **Deleted from the BCF:**
  - guaifenesin 600 mg extended (sustained) release tablets
- **Considered for BCF addition, but not added:**
  - escitalopram (Lexapro; Forest Labs)
  - methylphenidate extended release capsules (Metadate CD;

Celltech/Medeva)
    - zonisamide (Zonegran; Elan)
- **BCF listings clarified:**
    - paroxetine controlled release (Paxil CR; Glaxo SmithKline) excluded from paroxetine listing

Contracting Issues

- Generic contract awards, renewals, and terminations
- Drug Classes Under Discussion
    - Oral Bisphosphonates
    - Glaucoma Agents
    - Atypical Antipsychotics
    - Topical Immune Modulators
- Contract initiatives still pending: Leutinizing Hormone Releasing Hormone (LHRH) agonists (solicitation closed, award expected; triptans (solicitation issued); angiotensin receptor blockers (ARBs) (solicitation under development); statins, thiazolidinediones ("glitazones") (solicitation under development).
- A joint DoD/VA solicitation will not be issued for a nasal corticosteroid.

DoD P&T Committee Meeting (21 Nov 2002)

- Newly Approved Drugs
    - Added to the NMOP Formulary
    - Excluded from the NMOP Formulary
    - BCF Clarifications:
        - amoxicillin/clavulanate extended release tablets (Augmentin XR) excluded from BCF listing for amoxicillin/clavulanate
- Uniform Formulary Proposed Rule
- NMOP & Retail Network Quantity Limits for 5-HT3 Receptor Antagonists
- Controlled Distribution Drugs

DoD P&T Executive Council Meeting (20 Nov 2002)

BCF Changes (See Page 4 for a consolidated list of changes to the BCF and the NMOP Formulary)

Niacin extended release (Niaspan) replaces immediate release niacin on the BCF

The Council decided to add Niaspan to the BCF and delete immediate release niacin (MTFs may continue to have immediate release or other niacin products on their formularies). The decision was primarily based on increased use (Niaspan is now on about 40% of MTF

formularies); results of a DoD database analysis indicating that patients started on Niaspan tend to remain on therapy longer than those started on other niacin products (see sidebar); and responses from MTF providers (who were overwhelmingly in favor of adding Niaspan).

Loestrin FE (or generic equivalent) added to BCF as low estrogen alternative

After noting that previous attempts to contract for oral contraceptives met with limited success, the Council voted to add norethindrone/EE/ferrous fumarate 1/0.02 mg (Loestrin FE or its generic equivalent) to the BCF, which previously did not include a low estrogen (20 mcg ethinyl estradiol) oral contraceptive.

Timolol maleate gel-forming solution 0.25% and 0.5% added to BCF- specific product is Timoptic XE (mandatory source contract)

The Council added Timoptic XE to the BCF; timolol ophthalmic solution is already listed.

Tolterodine extended release (Detrol LA) added to BCF

In June 2001 the Council discussed the drugs used for treating overactive bladder (OAB) in response to several requests to add Detrol LA to the BCF. At that time the Council concluded that none of the drugs offered sufficient clinical benefit to justify their significantly higher cost compared to oxybutynin immediate release.

At the November 2002 meeting, the Council added tolterodine extended release (Detrol LA) to the BCF after considering a number of factors: expert opinion concerning patient perception of benefit with these medications; increased usage of tolterodine extended release in the MHS; head-to-head data comparing tolterodine extended release to oxybutynin extended release; the results of a DoD database analysis which found higher refill rates with tolterodine extended release than with other OAB medications (see sidebar); and the manufacturer's offer of a blanket purchase agreement (BPA) reducing the price of tolterodine extended release if added to the BCF.

Addition of venlafaxine extended release capsules (Effexor XR) to the BCF finalized

DoD Database Analysis: Patients Remaining on Therapy with Niaspan vs. Immediate Release Niacin at 6 Months

The PEC identified niacin-naïve patients who started treatment with Niaspan or other niacins in January and February of 2002. Overall, 55% (1676/3044) of patients receiving Niaspan remained on therapy at least 6 months later, compared to 37% (282/769) of patients receiving other niacins.

Refill Rates for OAB Drugs

An analysis of PDTS data from Jul 01 to Oct 02 showed that 58.4% of patients prescribed Detrol LA obtained at least one refill of their prescription, compared to only 36.7% for Detrol, 36.1% for Ditropan XL, and 30.7% for oxybutynin immediate release. The higher refill rate for Detrol LA may indicate that patients tolerate it better than other agents and/or that patients perceive that it works better than the other agents.

At the August 2002 meeting, the Council voted to add venlafaxine extended release 37.5, 75, and 150 mg capsules to the BCF, contingent on the signing of a BPA between Wyeth-Ayerst and Defense Supply Center Philadelphia (DSCP) that would lower the price of the medication. The lower price has now been finalized (via a voluntary reduction in the FSS price rather than a BPA), so Effexor XR is now on the BCF and facilities are required to include it on their formularies.

Guaifenesin 600 mg extended release tablets deleted from the BCF

As of 12 July 2002, Adams Labs' brand of guaifenesin 600 mg extended release (Mucinex) became the first single ingredient guaifenesin extended release product to be 1) approved as safe and effective under a New Drug Application (NDA) and 2) to be approved as an over-the-counter (OTC) product. The FDA has determined that single ingredient guaifenesin extended release drug products are new drugs and require an approved application for marketing. As a consequence, the FDA sent warning letters to manufacturers and distributors of guaifenesin products in October 2002, explaining that currently marketed single ingredient guaifenesin extended release products without an approved application are considered misbranded and in violation of section 505(a) of the FDCA and requesting action plans to bring their products into legal compliance. In addition, OTC approval of Mucinex means that manufacturers can no longer market single ingredient guaifenesin extended release products as prescription drugs. It is not known if any single ingredient guaifenesin extended release product other than Mucinex will continue to be available in the near future.

At the May 2002 meeting, the Council reviewed the issue of OTCs on the BCF and decided not to add any additional OTC products to the BCF beyond those identified in the TRICARE Policy Manual (insulin products (look up)). The Council encouraged MTFs to continue providing OTC medications when they represent cost-effective alternatives to legend drugs. As a consequence, the Council deleted guaifenesin 600 mg extended release from the BCF. MTFs may decide whether or not to remove the product from their formularies. As an OTC product, Mucinex will not be available from the retail network or NMOP.

Considered for BCF addition, but not added: escitalopram (Lexapro; Forest Labs)

The DoD P&T Committee added escitalopram to the NMOP Formulary in May 2002, just prior to FDA approval, but review of escitalopram for the BCF was tabled until Nov 2002, following FDA approval and marketing. At the November 2002 meeting, the Council concluded that current evidence does not indicate that escitalopram offers significant clinical or economic advantages over citalopram or the other SSRIs currently on the BCF (citalopram, fluoxetine, paroxetine, and sertraline) and that the SSRIs currently on the BCF are more than adequate to meet the clinical needs of DoD beneficiaries. The Council decided not to add escitalopram to the BCF.

Considered for BCF addition, but not added: methylphenidate extended release capsules (Metadate CD; Celltech/Medeva)

The Council reviewed Metadate CD for inclusion on the BCF, secondary to new clinical information and a BPA offer from Celltech Pharmaceuticals in exchange for placement on

the BCF. Based on review of the new information, provider opinion, and the potential economic advantage that could realistically be obtained, the Council voted not to add Metadate CD to the BCF.

Considered for BCF addition, but not added: zonisamide (Zonegran; Elan)

The Council reviewed zonisamide for the BCF because of an MTF provider's request, which supported zonisamide as a useful and safe drug to use for diabetic peripheral neuropathy, chronic headache syndromes, restless leg syndrome, and chronic back pain. (All are off-label uses; zonisamide is approved by the FDA only as “adjunctive therapy in the treatment of partial seizures in adults with epilepsy.”) The Council voted not to add zonisamide to the BCF because of the lack of published data supporting its use in these conditions; safety and tolerability concerns; and lack of significant use of zonisamide in DoD (only 23 MTFs filled more than 6 zonisamide prescriptions in FY 02).

Paroxetine controlled release (Paxil CR; Glaxo SmithKline) excluded from the BCF listing for paroxetine.

The DoD P&T Committee added paroxetine controlled release to the NMOP Formulary in May 2002, but excluded it from the BCF listing for paroxetine because the information available at that time did not demonstrate that the controlled release formulation offered any significant advantages compared to immediate release paroxetine. Paroxetine controlled release was reviewed again at the November 2002 meeting. The Council concluded that current evidence does not indicate that paroxetine controlled release offers significant clinical or economic advantages over paroxetine immediate release or the other SSRIs currently on the BCF (citalopram, fluoxetine, paroxetine, and sertraline) and that the SSRIs currently on the BCF are more than adequate to meet the clinical needs of DoD beneficiaries. The Council excluded paroxetine controlled release from the BCF listing for paroxetine.

Contracting Issues

Contract Awards, Renewals, and Terminations

- **New contracts awarded:** albuterol inhalers (to Ivax) and lisinopril (to West-Ward). The lisinopril contract was effective 21 Nov 02 for bottles of 100, but will not be effective for bottles of 1000 until Mar 03 due to a short supply of raw materials.
- **Contracts not awarded because the bid prices were higher than existing FSS prices:** penicillin, amoxicillin, dicloxacillin, cephalexin
- **Being solicited:** tretinoin cream
- **A note about generic contracts:** The Council received a report that some solicitations for joint DoD/VA generic contracts do not elicit competitive bids because the generic companies have trouble meeting the large demand from both agencies. The Council noted that standardization is needed by both agencies, particularly to support the use of automation, and suggested that the two agencies

might be more successful by pursuing separate contracts to avoid overwhelming the production capabilities of the generic manufacturers.

See **DSCP's DMM-Online website** for a **complete list of DoD and DoD/VA contracts, including contract prices and NDCs**. Questions regarding DoD and joint DoD/VA contracts should be directed to MAJ John Howe at DSCP or LCDR Ted Briski at the PEC.

Oral Bisphosphonates

After reviewing therapeutic interchangeability, clinical coverage, and provider acceptance, the Council concluded that alendronate (Fosamax; Merck) and risedronate (Actonel; Proctor & Gamble/Aventis) appear to have similar efficacy in reducing fractures and similar safety and tolerability and that either agent would likely meet the clinical needs of more than 90% of the population requiring treatment. They noted that 48 of 55 providers responding to a PEC survey were willing to use either agent equally in patients newly started on therapy, while 43 of 59 providers were willing to switch current patients to the selected agent if the switch could be done at a regularly scheduled visit rather than incurring an extra visit. Both alendronate and risedronate are now available in daily or weekly dosing formulations (with the weekly formulations accounting for the majority of DoD usage). DoD spends about $5 million a month on oral bisphosphonates across all outpatient pharmacy points of service (MTFs, mail order, and retail network pharmacies).

The Council voted unanimously to support any contracting/formulary strategy (to include a closed class contract with patient switches) designed to lower the cost of bisphosphonate drug therapy for DoD.

Glaucoma Agents

High utilization of latanoprost (Xalatan) and timolol maleate gel-forming solution (Timoptic XE & generics), which are not currently on the BCF, as well as the availability of new products for the treatment of glaucoma, triggered the Council's review of glaucoma agents on the BCF. The PEC also received a request from the field to delete pilocarpine from the BCF due to low utilization.

Prior to the meeting, the BCF included the following glaucoma medications:

- Timolol 0.25% and 0.5% ophthalmic solution (Alcon Labs brand only- DoD mandatory source contract), a topical beta-blocker
- Brimonidine 0.15% ophth soln (Alphagan P), a sympathomimetic agent
- Pilocarpine ophthalmic solution, a miotic agent.

The Council decided to add timolol gel-forming solution (Timoptic XE), 0.25% and 0.5%, to the BCF. (Although generically available, a DoD mandatory source contract has been awarded to Merck for the Timoptic XE brand.) Timoptic XE has a higher utilization rate than the contracted timolol ophthalmic solution; may be dosed once daily, potentially increasing

compliance; and has a current contract price comparable to the ophthalmic solution. The Council voted to maintain pilocarpine ophthalmic solution on the BCF; although utilization is low, pilocarpine has a unique place in therapy for the treatment of acute closed angle glaucoma. The Council agreed that carbonic anhydrase inhibitors (e.g., acetazolamide) would not be considered for inclusion on the BCF due to low utilization and poor tolerability.

The remaining class of glaucoma agents not currently represented on the BCF are the prostaglandins (latanoprost, bimatoprost, travoprost, and unoprostone). At the time of the meeting all of these agents were indicated for reduction of elevated intra-ocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension who are intolerant of other IOP-lowering medications or insufficiently responsive to another IOP-lowering medication. (Latanoprost has subsequently received an indication as an initial treatment for elevated eye pressure associated with open-angle glaucoma or ocular hypertension.) Utilization of ophthalmic prostaglandin agents is increasing, costs are high, and there appears to be the potential for price competition in this class due to the number of competing agents available. After considering efficacy, safety/tolerability, therapeutic interchangeability, clinical coverage, and provider acceptance in this drug class, the Council voted to add a prostaglandin to the BCF utilizing a closed class contracting strategy competing latanoprost, bimatoprost and travoprost. The contract would not require patients to be switched from one agent to another (providers were uniformly opposed to any contract requiring patient switches).

Atypical Antipsychotics

In November 2001, the DoD P&T Executive Council removed oral haloperidol from the BCF due to decreasing utilization and the perception that primary care providers in the outpatient setting do not commonly prescribe antipsychotics. The BCF does not currently include any agents approved specifically for the treatment of psychosis. The PEC has received two requests from MTF providers to add one or more atypical antipsychotics to the BCF (one for olanzapine and one for olanzapine and risperidone). Requestors argued that: atypical antipsychotics are first-line agents in treating psychotic manifestations of psychiatric disorders, they are utilized by civilian and military psychiatrists and should be readily available for continuation treatment, and typical antipsychotics are no longer standard of care for patients who need long-term therapy.

After considering provider opinion; increasing utilization of atypical antipsychotics at MTFs (both in absolute terms and relative to typical antipsychotics), the formulary status of atypical antipsychotics at MTFs (69 of 102 facilities analyzed had at least one atypical antipsychotic on formulary); and efficacy and safety of atypical antipsychotics relative to typical antipsychotics, the Council agreed that one or more atypical antipsychotic agents are needed on the BCF. The Council asked the PEC to complete its review of the atypical antipsychotics and make a specific recommendation at the next meeting regarding the number of agents that should be added, and which agent(s) represent the most cost-effective choice.

Topical Immune Modulators

This new class of topical, nonsteroidal medications is indicated for the treatment of atopic dermatitis (AD). Two agents are currently available: tacrolimus (Protopic), which is FDA

approved for treatment of moderate to severe AD, and pimecrolimus (Elidel) , which is FDA approved for the treatment of mild to moderate atopic dermatitis. The Council reviewed the TIMs due to an MTF provider's request to add pimecrolimus to the BCF. They noted the following:

- Because they are not sytemically absorbed, TIMs have advantages compared to long-term topical corticosteroids (avoidance of adverse effects associated with long-term topical corticosteroids and ability to use in sensitive body areas such as the face and intertriginous areas).
- Provider response was markedly positive regarding the potential of having an alternative to topical steroids for patients that require one. At the same time, providers noted that these will not take the place of the low potency topical corticosteroids and the usual initial therapies for mild AD.
- Usage of TIMs is increasing in all points of service (MTF, NMOP, and retail), with the majority of use in the very young (ages 0 - 4) and elderly (ages 65+) population. Providers feel that usage will continue to increase significantly in this class.

The Council agreed that topical immunomodulators (TIMS) are a unique class and have a substantial place in therapy for the treatment of AD; however, there is concern regarding the cost of these agents and the potential for misuse. The Council agreed to consider one or both of these medications for addition to the BCF at their next meeting. They asked the PEC to explore procurement options and report back in three months.

Contract initiatives still pending: Leutinizing Hormone Releasing Hormone (LHRH) agonists (solicitation closed, award expected; triptans (solicitation issued); angiotensin receptor blockers (ARBs) (solicitation under development); statins, thiazolidinediones ("glitazones") (solicitation under development).

A joint DoD/VA solicitation will not be issued for a nasal corticosteroid.

DoD P&T Committee Meeting (21 Nov 2002)

Newly Approved Drugs – See the New Drug Watch article on **Page 7** of this issue of the *PEC Update* and Appendix A of the **Nov 02 DoD P&T Committee minutes** for more information on the drugs.

Added to the NMOP Formulary

- Augmentin/clavulanate acid extended release tablets (Augmentin XR; GSK)
-

Clindamycin 1%/benzoyl peroxide 5% topical gel (Duac; Steifel Labs)

- Glipizide / metformin tablets (Metaglip; BMS)
- Rosiglitazone/metformin tablets (Avandamet; GSK)
- Dutasteride tablets (Avodart; GSK)
- Ethinyl estradiol 25 mcg/norgestimate (varying doses) tablets (Ortho Tri-Cyclen Lo; Ortho McNeil)
- Alosetron tablets (Lotronex; GSK) – **NOTE:** the controlled distribution program requirements for alosetron can be met through the NMOP, however faxed prescriptions cannot be accepted
- Tegaserod tablets (Zelnorm; Novartis)
- Adefovir tablets (Hepsera; Gilead)
- PEG interferon alfa-2a injection (Pegasys; Roche) – added to the NMOP Covered Injectables List
- Ezetimibe tablets (Zetia; Merck)

Excluded from the NMOP Formulary

- Avage brand of tazarotene 0.1% topical cream (Allergan) – specifically excluded from the NMOP Formulary, since its use is limited to cosmetic applications; other drugs intended solely for cosmetic use as a result of the aging process are not available from the NMOP.

BCF Clarification:

- Amoxicillin/clavulanate extended release tablets (Augmentin XR) excluded from BCF listing for amoxicillin/clavulanate

Uniform Formulary (UF) Proposed Rule

The comment period for the UF proposed rule has closed. The TMA Pharmacy Program Office is currently in the process of formulating responses to comments submitted by the public.

NMOP and Retail Network Quantity Limits for 5-HT3 Receptor Antagonists

In response to a beneficiary complaint, the Committee reviewed the current NMOP and retail network quantity limits for oral 5-HT3 receptor antagonists. The current quantity limits were established in Aug 99 based on the drug's use for the FDA-approved indication: the prevention or treatment of chemotherapy

induced nausea or vomiting. Since the quantity limits were initially established, the FDA has approved ondansetron and granisetron for use in the prevention or treatment of nausea and vomiting associated with radiation therapy and has approved ondansetron and dolasetron for treatment of postoperative nausea and vomiting. While the latter indication requires no modification in the quantity limit, the former could be associated with the use of a substantially greater number of tablets than specified by the current quantity limits.

After reviewing data comparing the number of tablets dispensed per prescription in each point of service to the established quantity limits, the Committee agreed that while the current quantity limits are not likely to be sufficient to meet the clinical needs of patients undergoing radiation therapy, it does not appear that this creates a significant problem for patients. This is most likely due to two factors: 1) the number of patients requiring treatment with antiemetics during their radiation therapy is low (studies have suggested that only patients receiving higher dose abdominal radiation and some patients receiving radiation therapy to the head and neck will require antiemetic therapy) and 2) a fair and effective review process exists for approval of prescriptions that exceed the established quantity limits (supported by the fact that only one complaint has been forwarded to the PEC in the three years since the quantity limits were established). Given the growing number of 5-HT3 receptor antagonist prescriptions being written for off-label indications such as hyperemesis gravidarum, the committee felt it would not be prudent to increase the quantity limits above the current levels, as these prescriptions should all be reviewed for clinical appropriateness.

Where to Find the Uniform Formulary Proposed Rule

The UF Proposed Rule was published in the Federal Register, Vol 67, No 71, FRI 12 Apr 2002; Civilian Health and Medical Program of the Uniformed Services. (Try going to the Federal Register by GPO Access page, (**www.gpo.gov/su_docs/aces/aces140.html**), checking the boxes for Vol 67 and "proposed rules", and specifying 04/12/2002 and some or all of the term "Civilian Health and Medical Program of the Uniformed Services" in the search boxes.)

Controlled Distribution of Prescription Drugs

Gamma hydroxy butyrate solution (Xyrem) has been approved by the FDA with distribution limited to a single pharmacy, Express Scripts' Specialty Distribution Services. Since Express Script's Specialty Distribution Services may not be a member of each MCSC network, patients will likely have to file out-of-network claims to get reimbursed for this drug. The MCSC Pharmacy Directors will look into enrolling Express Scripts into their networks so only a copay will be required. Information about specific drugs subject to controlled distribution programs is available on the PEC website. LCDR Ted Briski (**Ted.Briski@amedd.army.mil**) is the PEC point of contact for distribution issues.

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Summary of Changes to the Basic Core Formulary and National Mail Order Pharmacy Formulary

Resulting from the 20-21 November 2002 meetings of the DoD Pharmacy & Therapeutics Executive Council and the DoD Pharmacy & Therapeutics Committee

1. BCF Changes

A. Additions to the BCF

1. Tolterodine extended release capsules (Detrol LA)
2. Timolol maleate, solution, gel-forming 0.25%, 0.5% (Timoptic XE; Merck brand only - mandatory source contract)
3. Norethindrone/EE/ferrous fumarate 1/0.02 mg (Loestrin FE or its generic equivalent [Microgestin FE])
4. Niacin extended release tablets (Niaspan)
5. Venlafaxine extended release capsules (Effexor XR)

B. Deletions from the BCF

1. Niacin immediate release oral
2. Guaifenesin 600 mg extended (sustained) release tablets

C. Changes and clarifications to the BCF - none

D. Exclusions from the BCF

1. Paroxetine controlled release (Paxil CR) was excluded from the BCF listing for paroxetine
2. Amoxicillin/clavulanate extended release tablets (Augmentin XR) excluded from the BCF listing for amoxicillin/clavulanate acid oral

2. NMOP Formulary Changes

A. Additions to the NMOP Formulary

1. Augmentin/clavulanate acid extended release tablets (Augmentin XR; GSK)
2. Clindamycin 1%/benzoyl peroxide 5% topical gel (Duac; Steifel Labs)
3. Glipizide / metformin tablets (Metaglip; BMS)
4. Rosiglitazone/metformin tablets (Avandamet; GSK)
5. Dutasteride tablets (Avodart; GSK)
6. Ethinyl estradiol 25 mcg/norgestimate (varying doses) tablets (Ortho Tri-Cyclen Lo; Ortho McNeil)
7. Alosetron tablets (Lotronex; GSK) – The controlled distribution program requirements can be met through the NMOP, however faxed prescriptions cannot be accepted.
8. Tegaserod tablets (Zelnorm; Novartis)
9. Adefovir tablets (Hepsera; Gilead)
10. PEG interferon alfa-2a injection (Pegasys; Roche) – added to the NMOP Covered Injectables List
11. Ezetimibe tablets (Zetia; Merck)

B. Exclusions from the NMOP Formulary -

1. Avage brand of tazarotene 0.1% topical cream (Allergan) – specifically excluded from the NMOP Formulary, since its use is limited to cosmetic applications; other drugs intended solely for cosmetic use as a result of the aging process are not available from the NMOP.

C. Removed from the NMOP Formulary; no longer available from the NMOP

1. Single ingredient guaifenesin extended release tablets – approved as an OTC product 12 July 02

D. Clarifications to the NMOP Formulary - None

3. Quantity Limit Changes (NMOP and retail network) - None

4. Changes to the Prior Authorization Program (NMOP and Retail Network) - None

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Update on the Changeover to the TRICARE Mail Order Pharmacy (TMOP) Program

Time is marching onwards toward the 1 Mar 03 changeover from the National Mail Order Pharmacy (NMOP) program to the TRICARE Mail Order Pharmacy (TMOP) program. New developments:

- As of 15 Jan 2003, DoD beneficiaries are able to pre-register with the TMOP on the Express Scripts website: **www.express-scripts.com** (click on the DoD seal). Additional information will be available from this site in the near future.

- More information concerning the TMOP is becoming available:
  - TMOP program information is now posted on the TRICARE website at **www.tricare.osd.mil/pharmacy/tmop.cfm**. Be sure to click on the FAQ link under "Get answers to the most common questions about TMOP."
  - TMOP information and/or links to other resources may also be accessed through the PEC website at **www.pec.ha.osd.mil/TMOP/tmop.htm**. Formulary information for the TMOP will be available from the PEC website when the program goes into effect on 1 Mar 2003. Information on the current NMOP Formulary (which will carry over to the new program) is available at: **www.pec.ha.osd.mil/NMOP/NMOPhome.htm**.
  - A TMOP slide show has been sent to the pharmacy service consultants/specialty leaders for distribution to the field.

- Beneficiaries currently using the NMOP will receive information about TMOP prior to its start date. Effective dates for beneficiaries are:
  - **15 January 2003** - Beneficiaries may register or subscribe at **www.express-scripts.com**
  - **1 February 2003** - Call center opens – toll-free: 1-866-DOD-TMOP (1-866-363-8667); outside the U.S. or U.S. territories: 1-866-275-4732
  - **1 February 2003** - details mailed to beneficiaries
  - **1 March 2003** - TMOP begins operation

- The Express Scripts fax number for the TMOP (for providers only) will be: 1-877-895-1900.


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Barb's Barbs

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Mumbo - Jumbo

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This piece was inspired by a phone call from a pharmaceutical representative who was upset about questionable information being presented to providers by a rival pharmaceutical company. I won't go into the details of the conversation but the rep asked if the PEC could write a policy or something to stop the practice. Both of us know that the PEC is not a policy-making organization, but we decided that this and similar events would be a good topic for a *PEC Update* article, so here goes.

One thing I've learned since I've come to the PEC is not to take anyone's word at face value. I want proof, and when I'm really thinking, I ask to see it in writing. There's a tired old phrase from the 60's that said, "What you see is what you get." Unfortunately what you hear is not always what they mean. Here are a few examples. I've made some up (based on a composite of e-mails and phone conversations I've had) and pulled some out of magazines, newspaper ads, journal articles etc.

What they say:	What you hear:	What they mean:
"Our drug is on the DoD formulary."	"Our drug is on the BCF."	"Our drug is available in the NMOP and retail points of service (that part of the DoD formulary, but not the actual BCF)."
"Our study used subspecialists because primary care docs don't know how to use this drug correctly."	"Primary care docs are too clueless to take care of patients appropriately with our drug."	"We used subspecialists because they see a ton of patients with this medical condition, so it's easier to get to our precalculated number to power this study right, but, boy, I really stuck my foot in my mouth when I said what I did."

“There is a sole source contract for our product.”	“I have to buy this stuff, too now? I don’t see it on the BCF.”	“Your region (MTF, doc, pharmacist, logistics – you fill in the blank here) is causing confusion by contracting separate from everyone else and our company is going to take advantage of that confusion.”
“Our new antibiotic, gorillaoxilactafloxmycillin, is FDA-approved for treatment of acute bronchitis and sinusitis.”	“I guess it is okay to use an antibiotic for these predominantly viral oriented diseases.”	“I hope the provider is impressed with the FDA indication we got for the weak study that didn’t include any placebo arm for a disease that doesn’t need an antibiotic in the first place.”
“Our study demonstrated a statistically significant result over placebo on the Mumbo-jumbo subscale.”	“This drug must be superior to placebo.”	“Our drug was statistically significant to placebo when we chose an outcome that has little to no clinical significance.”
“This fabulous infomercial offer is only valid if you call in the next 10 minutes!”	“Where’s the phone? This is an emergency. I’ve got to call now.”	“Time is relative. Call now. Call later. We’ll take your money anytime, sucker.”
“Thank you for this interesting consult.”	“Wow, the specialist thought this was a cool patient and now that I’ve dumped on him, I can be OTD (out the door) for my weekend trip.”	“Thanks for the dump. This consult is about as interesting as a Code Brown*. I’ll get you back soon.”
“There are no head-to-head studies between our drug and Drug X.”	“There are no head-to-head studies because you don’t want to find out that your drug is really no different than the competition.”	“There are no head-to-head studies because we don’t want to confirm that our drug is really no different than the competition. That’s not good for marketing.”

"The potential cost-avoidance for DoD is $2 million if the DoD P&T Executive Committee will consider 'Xclearolungo' for the BCF instead of opting for its competitor, 'Propelophlegmzz.'"	"The potential cost-savings for DoD is $2 million dollars by choosing one drug over the other. Where does that extra money go to?"	"The potential cost-avoidance is ….blah blah blah. Cost-avoidance is not the same as cost-savings. If **you** choose to buy a Yugo instead of a Ferrari, **you've** avoided spending a lot of bucks (if you actually have the bucks to spend) that can now be spent on something else. **You** don't get some magic kickback or slush fund by not spending the money. Hey guess what? Neither do we!"
"Wow, Barb. I really liked your last article."	"What a dweeb. I bet I could sell them tickets for an all expenses paid vacation to Pluto."	"Don't quit your day job."
*Code Brown: Medical slang for a particularly onerous medical student (usually) duty. It's manual disimpaction of a constipated patient.		

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How to Identify the Research Design of a Study

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Previous articles in this series

Epidemiology: What's Pharmacy Got to Do With It?

In the October *PEC Update*, CDR Graham discussed some of the ways in which epidemiology relates to pharmacy research. In this issue, I am going to discuss a related topic—a method to help identify the research design of a study.

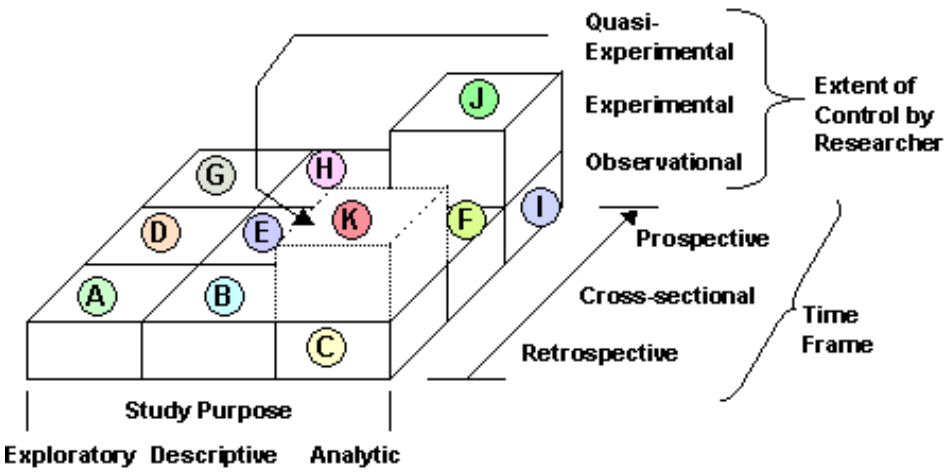
In the third edition of *A Dictionary of Epidemiology*, John M. Last[1] defines **research design** as **"the procedures and methods, predetermined by an investigator, to be adhered to in conducting a research project."** In other words, the research design could be thought of as the set of rules that establishes the procedural boundaries for the study. For the researcher, the rules apply to how the study is conducted. For those in the field reading the study, the rules apply to how the results are interpreted and generalized.

A number of different approaches have been used to classify research designs. One approach that I have found to be particularly useful and easy to use is the classification system developed by Burkett.[2] This system is based on a three-dimensional framework consisting of axes that represent:

1. the **purpose** of the study
2. the **time frame** over which the study was (or will be) conducted
3. the **extent of control** the investigator has over the study variables

Using this framework, a two-step process can be used to identify the study design. The first step involves making an independent decision regarding the position of the study along each of the three axes and the second involves identifying the point or cell within the three dimensional model in which the positions of the three axes intersect. This three dimensional approach is illustrated in Figure 1.

Figure 1: Burkett's Classification System



Adapted from: Burkett GL. Classifying basic research designs. Family Medicine 1990;22;143-148

Legend: Examples of studies that can be included in each cell – not exhaustive

- A Literature reviews
- B Quality assurance chart audits
- C Case-control studies
- D Single semi-structured interviews
- E Parts of most surveys
- F Parts of most surveys
- G Longitudinal participant observation
- H Longitudinal case study
- I Prospective cohort study
- J Randomized clinical trial
- K Quasi-experimental study

Study Purpose

The study purpose can be classified as **exploratory, descriptive, or analytic.**

- **Explanatory** studies are most commonly used to generate hypotheses or to clarify or better define questions that could be used in future research. Exploratory research is generally conducted when the information available about a subject is insufficient to conduct a descriptive or analytic study.
- **Descriptive** research is also used to generate hypotheses but generally has more information available than in exploratory research. Descriptive research is usually conducted to characterize one or more variables within a population, particularly in relation to person, place, and time.
- **Analytic** research, on the other hand, is generally associated with the testing of a hypothesis. This usually involves an intervention in which two or more variables are compared or contrasted. The primary purpose of an experimental design is to determine the extent of causality between the variables under investigation.

Time Frame Under Investigation

Research can be conducted in one of three time periods: **retrospective, cross-sectional, or prospective.**

- In **retrospective** research the investigator looks backward from the present time to examine a historical event or a chain of historical events. An example of this type of study would be the *case-control* study in epidemiology.
- **Cross-sectional** research measures responses at a single point in time. Survey research frequently utilizes the cross-sectional time frame.
- In **prospective** research**,** the investigator follows a group of subjects forward in time to determine results. Randomized clinical trials,

or a prospective cohort study, are examples of research designs that utilize this type of time frame.

Extent of Investigators' Control Over Study Variables

This axis refers to the degree or extent to which the investigator has control of the research intervention. Burkett discusses two primary designs: **observational and interventive (experimental).**

- In **observational** studies, the investigator simply observes the natural course of events and records the results without trying to influence them.
- On the other hand, **interventive (experimental)** studies require the investigator to become an active participant by introducing an intervention that affects at least some of the subjects in the study and allows for some judgment of a causal relationship between the intervention and one or more other variables of interest.

Although not discussed by Burkett, I have also illustrated the way in which a **quasi-experimental** design might fit into this framework (look for the dotted lines in Figure 1). The retrospective aspect of quasi-experimental design prohibits the introduction of direct interventions; however, the researcher can still achieve a certain level of experimental control by choosing comparator groups based upon exposure or non-exposure to an event or intervention. An example of this might be the use of a retrospective database to compare outcomes between asthmatics treated according to clinical practice guidelines (the exposure group) and those not treated according to clinical practice guidelines (the non-exposure group).

This article is not intended to be a complete review of study design schemas, just a useful starting point to identify the research design of studies. For a more complete explanation of Burkett's classification system and methods for identifying research designs please refer to the following references.

References

1. Last JM. A Dictionary of Epidemiology. Third Edition, 1995 International Epidemiological Association, Oxford University Press, NY, NY

2. Burkett GL. Classifying basic research designs. Family Medicine 1990;22:143-8.

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New Drug Watch

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This month: new agents for ADHD and osteoporosis, a combination vaccine (diphtheria, tetanus, pertussis, hepatitis B, and polio), a handful of new formulations and indications, generic omeprazole, FDA alerts, updated neonatal group B streptococcus prophylaxis recommendations and results of some notable trials, including ALLHAT (the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial).

Newly Approved Drugs From Head to Toe

Neurology / Psychiatry

Atomoxetine (Strattera; Lilly) has received FDA approval for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adults. This drug is a selective norepinephrine reuptake inhibitor and not a stimulant, thus it does not fall under the category of a controlled substance. Atomoxetine is metabolized via the CYP2D6 pathway, and has potential for drug interactions with 2D6 inhibitors (e.g., fluoxetine, paroxetine, quinidine). Additionally, atomoxetine should not be taken with monoamine oxidase inhibitors (MAOIs) because of reports of potentially fatal reactions. Approval for treating adults was based on the results of two placebo-controlled clinical trials that enrolled about 500 patients; 4 trials were conducted to evaluate pediatric/adolescent use. Dosing of atomoxetine is weight-based for children/adolescents weighing less than 70 kg. For adults, therapy is initiated at a dose of 40 mg daily, given as a single dose or in divided doses (morning and early afternoon). Atomoxetine capsules are available in 5-, 10-, 18-, 25-, 40-, or 60-mg strengths. Launch is expected in Jan 03.

Endocrinology

A new osteoporosis treatment, **teriparitide injection (Forteo; Lilly)**, was approved in Nov 02. Labeled indications for teriparitide are limited to men or postmenopausal women at high risk of having a fracture. The 20 mcg daily dose is administered SQ in either the thigh or

abdomen. It is available in a 3 mL pre-filled pen that requires refrigeration and supplies 28 doses, after which the pen should be discarded (even if unused solution remains). Teriparitide is a recombinant parathyroid hormone (PTH), which stimulates new bone formation by increasing osteoblast activity. Concomitant calcium and vitamin D supplementation is recommended. A black box warning outlines the possible risk of cancer formation with teriparitide, since rodent studies showed an association with osteosarcoma. A mandatory medication guide discussing this issue should be given to the patient when the drug is dispensed. Treatment duration is limited to two years, due to the unknown long-term adverse event profile. Initially, Lilly will only be detailing the drug to 8000 physicians specializing in osteoporosis, as part of a risk management program to ensure that only patients at high risk of fracture are prescribed teriparitide. Teriparitide will not be advertised directly to the consumer.

Infectious Diseases

An extended release preparation of ciprofloxacin **(Cipro XR, Bayer)** was approved on 16 Dec 02. It is labeled for once daily treatment of uncomplicated UTIs (acute cystitis), for a duration of 3 days. Availability is expected in Jan 03.

Pediatrics

A combination vaccine containing DtaP (diphtheria, and tetanus toxoids and acellular pertussis vaccine adsorbed), recombinant hepatitis B, and inactivated polio virus received FDA approval 16 Dec 02. The brand name is **Pediarix (Glaxo SmithKline)**. The combination vaccine contains two previously marketed components from Glaxo SmithKline, Engerix-B and Infanrix. A three-dose series is recommended for infants at age 2, 4, and 6 months.

New OTC Meds

A **second OTC loratidine product** is now available. The brand name is Alavert (Wyeth Consumer Healthcare). The product is available as 10 mg orally disintegrating tablets.

New Indications

Roche's pegylated interferon product, **PEG interferon alfa-2a (Pegasys)**, is now approved for combination use with ribavirin (Copegus) for treatment of chronic hepatitis C virus in patients who have compensated liver disease and who have not been previously treated with alfa interferon. The PEG interferon alfa-2a dose is 180 mcg administered SQ once weekly; the ribavirin dose is 800 to 1200 mg given in divided doses, based on viral genotype. Duration of therapy (24 weeks or 48 weeks) is also based on viral genotype. Peginterferon alfa-2a was originally approved on 18 Oct 02 for use as monotherapy. Copegus is the Roche trademarked name for ribavirin; Schering markets their formulation of ribavirin under the Rebetol brand name.

New Formulations

Escitalopram (Lexapro; Forest) is now available in an oral solution. Launch is anticipated in Jan 03.

New Generics

Omeprazole is (finally) available generically, following years of litigation between Astra Zeneca, the manufacturer of Prilosec, and several generic pharmaceutical companies. Kremers Urban Development Company (Kudco), a division of Schwarz Pharma, is marketing the product. The Dec 18th edition of the Pink Sheet noted that generic omeprazole will not be available to mail order pharmacies, since the manufacturer can only supply about 50% of the expected demand. The product will be supplied to wholesalers and retail pharmacies. An OTC formulation of omeprazole (Prilosec 1; Astra Zeneca) has been held up at the FDA, pending completion of studies verifying consumer comprehension of labeling. Final approval is not expected until late 2003.

Market Withdrawals

- **Cefixime (Suprax, Wyeth)**, which lost patent protection in Nov 02, has been discontinued by the manufacturer. The supplies of the 200 and 400 mg tablets have been depleted; however, supplies of the suspension (100 mg/5 mL) are expected to last until Mar 03. There are no FDA-approved generic cefixime formulations. The CDC issued an alert on this issue, as cefixime is the only antibiotic to which resistance to *N. gonorrhoeae* has not developed. With the discontinuation of cefixime, treatment recommendations for uncomplicated *N. gonorrhoeae* are ceftriaxone 125 mg IM, or oral fluoroquinolones. In Asia and the Pacific Islands (which includes Hawaii and California), fluoroquinolone resistance to *N. gonorrhoeae* is problematic, thus the CDC recommends ceftriaxone. For pediatric patients and pregnant women, ceftriaxone is the drug of choice. [Consult the CDC's Morbidity and Mortality Weekly Report (MMWR) 2202; 51:1052 (**www.cdc.gov/mmwr/preview/mmwrhtml/mm5146a6.htm**) or the CDC's National Center for HIV, STD and TB Prevention website (**www.cdc.gov/nchstp/dstd/dstdp.html**) for more information.

- The migraine treatment **methysergide (Sansert; Novartis)** has been discontinued. Remaining supplies are expected to be depleted in Feb 03. Methysergide has been associated with severe effects of retroperitoneal fibrosis, pulmonary fibrosis, and thickened cardiac valves.

FDA Alerts

The FDA issued an alert regarding importation of 10 drugs from overseas, or ordering from Internet websites. These 10 drugs all have safety issues and restricted/controlled distribution programs or required laboratory monitoring schedules. FDA feels that importing these drugs would negate the safety programs in place. The drugs are the following:

- **Isotretinoin (Accutane)** capsules – potential for teratogenicity; psychiatric side effects; controlled distribution program
- **Oral transmucosal fentanyl citrate (Actiq)** – potential for respiratory depression, accidental use

in children ("lollipop" dosage form)
- **Clozapine (Clozaril)** tablets – mandatory CBC monitoring
- **Lotronex (Alosetron)** tablets – potential for ischemic colitis and severe constipation; controlled distribution program
- **Mifepristone (Mifiprex)** tablets – potential for ruptured ectopic pregnancy
- **Thalidomide (Thalomid)** capsules – potential for teratogenicity; controlled distribution program
- **Dofetilide (Tikosyn)** capsules – potential for arrythymias, controlled distribution program
- **Bosentan (Tracleer)** tablets – potential for teratogenicity, hepatotoxicity; controlled distribution program
- **Trovafloxacin tablets or alatrofloxacin injection (Trovan)** – potential for hepatotoxicity; use restricted to inpatient care.
- **Sodium oxybate (Xyrem)** oral suspension – potential for diversion; restricted distribution program

New Guidelines

Neonatal group B streptococcus (GBS) prophylaxis recommendations have been updated by the CDC (**http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5111a1.htm**). The guidelines were first published in 1996. Changes to the guidelines include the recommendation for universal prenatal screening for rectal and vaginal GBS colonization in all pregnant women at 35-37 weeks gestation and updated suggestions for prophylaxis of patients with penicillin allergy.

New Studies of Note

Hypertension – thiazide diuretics are proven first-line agents

The much anticipated results of the **ALLHAT** (Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) were announced in the Dec 18th issue of JAMA (**http://jama.ama-assn.org/issues/v288n23/abs/joc21962.html**). Over 40,000 patients were enrolled in the trial, which compared a diuretic (chlorthalidone), angiotensin converting enzyme inhibitor (lisinopril), calcium channel blocker (amlodipine) and alpha blocker (doxazosin). Follow-up continued for approximately 5 years. The doxazosin arm was stopped prematurely in Jan 00 due to a higher number of cardiovascular events and hospitalizations for CHF than chlorthalidone. There was no difference between the remaining three treatments in terms of coronary heart disease death or nonfatal MI. Chlorthalidone showed superiority in several secondary endpoints (all-cause mortality, fatal and nonfatal stroke, combined CHD and combined cardiovascular disease).

Thiazide diuretics are now considered the initial drug of choice for hypertension, due to their benefits in preventing CHD, and low cost. For patients already receiving antihypertensive therapy, a diuretic should be considered; most patients with hypertension will require more than one drug for adequate blood pressure control.

Chlorthalidone was chosen based on its prior use in the SHEP (Systolic Hypertension study in Elderly Program) trial; whether the results of ALLHAT can be extrapolated to other thiazides, mainly HCTZ, is unknown. HCTZ is less potent than chlorthalidone, and doses of HCTZ 12.5 mg would not be equivalent to the 12.5-25 mg chlorthalidone doses used in

ALLHAT.

Merits of the ALLHAT study in addition to the large number of subjects were the enrollment of typical patients found in the "real world" – females, African Americans, diabetics, elderly, and Hispanics. Additionally, the primary outcomes are hard outcomes, and not surrogate markers, which are often seen in cardiovascular trials. The medical community considers this a landmark trial, and it is expected that the next update from the Joint National Committee (JNC) will reflect these results.

Just a word of caution: hypertension therapy should be individualized to the patient. While applicable to the typical geriatric internal medicine clinic patient, the results of ALLHAT may not be applicable to the active duty population. For example, diuretics may not be the best choice for active duty personnel in environments where dehydration is difficult to avoid.

Atrial Fibrillation – new studies now favor rate control over rhythm control

The National Institutes of Health (National Heart and Lung Blood Institute (NHLBI) issued a press release discussing the results of two studies (AFFIRM and RACE) published in the December 4th 2002 issue of New England Journal of Medicine. Over 4500 elderly patients with atrial fibrillation were enrolled in a North American and European study to examine the issue of rate control (digoxin, beta blockers, and/or calcium channel blockers) vs rhythm control (amiodarone, sotalol, propafenone, procainamide, quinidine, flecainide, disopyramide, moricizine, or dofetilide). In both studies, there was no difference in survival between the two treatments. Rhythm control was not found to reduce the risk of stroke, improve quality of life, reduce hospitalizations, or improve cognitive function. Rate control is now a primary approach (with anticoagulation) for atrial fibrillation, as antiarrhythmic therapy is associated with low efficacy rates, higher costs, and problematic adverse effect profiles. The NHLBI press release is available on the Internet at http://www.nhlbi.nih.gov/new/press/02-12-04.htm.

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PDTS Corner

Update on the Pharmacy Data Transaction Service

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PDTS - Looking Ahead While Glancing Back

By COL (Ret) Roger Williams, PDTS CSSC, Clinical Support Supervisor

Here we are starting a new year already. January is just a few days old, but what a year 2003 will be for DoD Pharmacy and our beneficiaries. The upcoming year will be significant for everyone working to provide an equitable and consistent pharmacy benefit to all DoD beneficiaries.

But before we look to the future, let's take a quick glance back and see the numbers for calendar year 2002.

PDTS Transactions & Potential Level 1 Drug-Drug Interactions Identified
Calendar Year 2002

Total transactions: 100,882,914*	**Potential Level 1 DDIs identified: 39,522**

Transaction results	**Level 1 DDIs reversed: 10.6%**
• **Paid: 91.30%** • **Reversals: 7.38%** • **Duplicate: 0.59%** • **Rejected: 0.74%**	• **by MTFs: 8.0%** • **by MCSCs: 10.8%** • **by NMOP: 20.8%**

(**Editor's Note**: Big number warning. That's over 100 **MILLION** transactions, or about 92 million prescriptions. If each one of these prescriptions were written on a prescription blank, you could stack them about 6 miles high. Theoretically.)

What can we expect in 2003?

In March we will see the launch of TMOP (the TRICARE Mail Order Pharmacy program), which will replace the NMOP (the National Mail Order Pharmacy program). This will result in a number of changes, including a new provider, Express Scripts Inc. While the pharmacy benefit itself will not change, a number of operational changes will improve services. Later this year we will see the solicitation for T-NEX (TRICARE the Next Generation), which will change the configuration of the TRICARE regions as we know them today and reduce the number of Retail Pharmacy Networks providing services.

Of course both of these new issues primarily impact our peacetime mission but we can't forget that the men and women in DoD Pharmacy have a readiness mission and they must be prepared whenever the time comes to deploy a fighting force. With all that is going on in the world today, that readiness mission may be closer than we would like. With that said, please keep in mind that PDTS and the Customer Service Support Center is ready to support DoD Pharmacy.

PDTS Data Integrity: a 2002 Review

By Teresa Dowell, PDTS CSSC, Clinical Support Coordinator

The Data Integrity project went full scale in June 2002. Since that time, we've seen vast improvements in the data transmitted—but there are still some issues. At first the majority of data integrity issues were within the drug file, specifically the package size. Now that we have addressed the package size issue, it seems that the majority of data integrity issues are created by user error or default sigs. The development team has implemented some changes to CHCS that have aided in fewer High Dose Alerts. Upon review of the changes, I would like to take the opportunity to pass on what has been recommended:

For all oral contraceptives, under **FRM**, leave the **DISPENSE COMPLETE CONTAINER** field **blank**. If this is filled in as **Yes**, the days supply will default to 30 days and show up as a PDTS warning for over-utilization. Of course, it will still show up as excessive days supply at #168 (Navy Policy), but that is a quick override.

If directions are typed in full words instead of using numbers, CHCS ignores them. Use **4** instead of **FOUR** if you want CHCS to understand the number.

If **PUFFS** is spelled out CHCS will miscalculate. Use **PF** instead. If the rest of the sig is correct, then the days supply should be reasonably accurate.

I would also like to mention the magnificent improvement that we see in the weekly Stoplight reports. It is quite obvious how hard sites are working on continuously improving the quality of service to our TRICARE beneficiaries. Thank you for your diligence and dedication in the ongoing data integrity effort.

Business Objects Class Schedule

By Beth Spearman, PDTS CSSC, Senior Reports Analyst

The capability to run reports on data in the PDTS Data Warehouse is now available to managers at various levels of DoD Pharmacy by using Business Objects software via an Internet Web Server. The PDTS Customer Service Support Center offers training sessions in Business Objects at Ft Sam Houston, Texas.

2003 Business Objects Class Schedule			
January	7–8	21-22	
February	11-12	25-26	
March	11-12	25-26	
April	8-9	22-23	
May	6-7	20-21	
June	3-4	17-18	
July	1-2	15-16	29-30
August	12-13	26-27	
September	9-10	23-24	
October	7-8	No second class due to Combined Forces	
November	4-5	18-19	

December	2-3	16-17	

Pharmacy personnel interested in attending a Business Objects training session need to obtain approval from their Service Consultant/Specialty Leader. An e-mail message showing approval sent to Beth Spearman or Roger Williams will suffice. All requests for training must be received at least two weeks prior to the date of training to allow time to process all paperwork and obtain passwords. For more detailed information please call 1-866-ASK4PEC (275-4732) or check out the **Business Objects page** in the PDTS section of the PEC website.

Top 10 Level 1 Drug-Drug Interactions by Point of Service

By COL (Ret) Roger Williams, PDTS CSSC, Clinical Support Supervisor

The feature in PDTS that enhances patient safety is the process of conducting Prospective Drug Utilization Reviews (ProDURs). PDTS conducts on-line ProDURs (clinical screens) on all medications dispensed, regardless of the DoD point of service the patient used to have the prescription filled. Pharmacy personnel need to be aware that with the activation of PDTS, the number of clinical screenings could increase depending on how frequently patients use multiple prescription sources. PDTS clinical screens are performed only on those medications the patient obtains from outside of the dispensing site's host cluster. It will not duplicate clinical warnings generated from within the CHCS host system.

For further information about the PDTS DURs, see **my article in the Mar 2002 PEC Update**.

Top 10 Potential Level 1 Drug-Drug Interactions in MTFs, November 2002

Rank	Medications involved	#
1	Ibuprofen / Ketorolac tromethamine	262
2	Ketorolac tromethamine / Naproxen	116
3	Nitroglycerin / Sildenafil citrate	86
4	Isotretinoin / Minocycline HCl	71
5	Ketorolac tromethamine / Rofecoxib	65
6	Celecoxib / Ketorolac tromethamine	60
7	Aspirin / Ketorolac tromethamine	42
8	Ketoconazole / Simvastatin	37

9	Isotretinoin / Doxycycline hyclate	33
10	Ketorolac tromethamine / Indomethacin	24

Top 10 Potential Level 1 Drug-Drug Interactions in the Retail Network, November 2002

Rank	Medications involved	#
1	Ibuprofen / Ketorolac tromethamine	106
2	Nitroglycerin / Sildenafil citrate	84
3	Ketorolac tromethamine / Naproxen	72
4	Isotretinoin / Minocycline HCl	68
5	Ketorolac tromethamine / Rofecoxib	61
6	Celecoxib / Ketorolac tromethamine	60
7	Ketoconazole / Simvastatin	36
8	Entacapone / Selegiline HCl	36
9	Isotretinoin / Doxycycline Hyclate	33
10	Amiodarone HCl / Gatifloxacin	23

Top 10 Potential Level 1 Drug-Drug Interactions in Mail Order, November 2002

Rank	Medications involved	#
1	Nitroglycerin / Sildenafil citrate	64
2	Intraconazole / Simvastatin	17
3	Ketoconazole / Simvastatin	15
4	Ketorolac tromethamine / Rofecoxib	14

5	Celecoxib / Ketorolac tromethamine	13
6	Amiodarone / Moxifloxacin	10
7	Entacapone / Selegiline	10
8	Ketorolac tromethamine / Valdecoxib	9
9	Fluoxetine / Selegiline HCl	8
10	Amiodarone HCl / Gatifloxacin	7

Top 50 Drugs in MTFs - Comparison with Retail and Mail Order

By Preston Hardy, PDTS CSSC Clinical Support Coordinator

One of the many benefits of PDTS is the capability to review and compare prescription utilization by point of service. This month's issue resumes our reports on the top 50 drugs (by prescription count) in each MHS point of service. Click on the link below to download the report for November 2002:

- **Nov 2002 MHS Top 50 Drugs by POS** (MS Excel)

The first three tables in the files list the top 50 drugs by prescription count dispensed at MTFs, the retail network, and the NMOP. Column headings are defined as follows:

- **Drug Description** - contains all strengths and dosage forms
- **Ranking** - from 1 (most dispensed) to 50 (least dispensed)
- **# of Rxs** - number of prescriptions dispensed
- **Qty. Disp.** - total quantity of measured units dispensed
- **Avg. Qty Per Rx** - average number of measured units per prescription
- **Avg. Days Supply** - average days supply issued per prescription
- **Unique Utilizers** - number of patients receiving a prescription for the listed drug from that point of service.

The fourth table compares the Top 50 drugs in MTFs against the same drugs in the retail network and NMOP. A blank cell means that the corresponding drug did not fall in the top 50 for that specific point of service.

The PDTS Customer Service Support Center

The PDTS CSSC strives to provide world-class customer support to all Military Health System users while enhancing the operational effectiveness and ensuring the quality of information maintained within the Pharmacy Data Transaction Service. The PDTS CSSC comprises the Pharmacy Benefit Operations Division of the PEC and is co-located with the Clinical Operations Division of the PEC at Ft. Sam Houston, TX.

The PDTS CSSC has an e-mail address for questions, comments, concerns, or report requests:

PDTS@cen.amedd.army.mil

Drop us an e-mail! We will respond via e-mail or call you within 1 business day.

Or call the PDTS CSSC at:

- **DSN: 471-8274**
- **Toll-free commercial:**
  1-866-275-4732
  (1-866-ASK4PEC)
- **Local commercial (San Antonio):**
  (210) 221-8274
- **OCONUS:**
  (AT&T access code)+866-275-4732

Need more information?

Many materials pertaining to PDTS, including trouble call procedures, the PDTS Report Request Form, business rules, and interchange control documents (ICDs), are available in the PDTS section of the PEC website. Just go to www.pec.ha.osd.mil/pdts/pdts_documents.htm and browse through the options on the left-hand navigation bar.

In addition, many articles on various aspects of PDTS and the PDTS CSSC have been published in recent issues of the PEC Update. Please visit the PEC Update page on the PEC website - www.pec.ha.osd.mil/ac03000.htm - for back issues.

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